with reference solution (e) or (f). If this test fails, adjust the injection volume between 10 µl and 20 µl, in order to be in the linearity range of the detector.

Calculate the content of insulin plus A21 desamido insulin from the area of the peak due to the bovine, porcine or human insulin and that of any peak due to the A21 desamido insulin, using the declared content of insulin plus A21 desamido insulin in bovine insulin CRS, porcine insulin CRS or human insulin CRS, as appropriate. For preparations containing both bovine and porcine insulin use the sum of the areas of both the bovine and porcine insulin peaks and of the peaks due to the A21 desamido insulin

STORAGE

Unless otherwise prescribed, store in a sterile, airtight, tamper-proof container, protected from light, at a temperature of 2 °C to 8 °C. Insulin preparations are not to be frozen.

LABELLING

The label states:

– the potency in International Units per millilitre,
– the concentration in terms of the number of milligrams of insulin per millilitre (for preparations containing both bovine insulin and porcine insulin the concentration is stated as the combined amount of both insulins),
– where applicable, the substance is produced by enzymatic modification of porcine insulin,
– where applicable, the substance is produced by recombinant DNA technology,
– where applicable, the animal species of origin,
– that the preparation must not be frozen,
– where applicable, that the preparation must be resuspended before use.

INSULIN ZINC INJECTABLE SUSPENSION

Insulini zinci suspensio injectabilis

Insulin zinc injectable suspension complies with the monograph on Insulin preparations, injectable (0854) with the amendments prescribed below.

DEFINITION

Insulin zinc injectable suspension is a sterile neutral suspension of bovine insulin and/or porcine insulin or of human insulin with a suitable zinc salt; the insulin is in a form which is practically insoluble in water.

PRODUCTION

Insulin zinc injectable suspension is prepared by carrying out the procedures described in the monograph on Insulin preparations, injectable (0854).

Insulin zinc injectable suspension is produced by mixing insulin zinc injectable suspension (crystalline) and insulin zinc injectable suspension (amorphous) in a ratio of 7 to 3.

CHARACTERS

A white suspension which on standing deposits a white sediment and leaves a colourless or almost colourless supernatant liquid; the sediment is readily resuspended by gently shaking. When examined under a microscope, the majority of the particles are seen to be rhombohedral crystals with a maximum dimension when measured from corner to corner through the crystal greater than 10 µm but rarely exceeding 40 µm; a considerable proportion of the particles are seen to have no uniform shape and a maximum dimension rarely exceeding 2 µm.

IDENTIFICATION

Examine the chromatograms obtained in the Assay. For preparations made from a single species of insulin (bovine, porcine or human), the positions of the peaks due to the two insulins in the chromatogram obtained with the test solution correspond to those of the principal peaks in the chromatogram obtained with the appropriate reference solution. For preparations made from a mixture of bovine and porcine insulin, the positions of the peaks due to the two insulins in the chromatogram obtained with the test solution correspond to those of the principal peaks in the chromatogram obtained with the appropriate reference solution.

TESTS

Insulin not extractable with buffered acetone solution: 63 per cent to 77 per cent of the total insulin content. Centrifuge a volume of the substance to be examined containing 200 IU of insulin and discard the supernatant liquid. Suspend the residue in 1.65 ml of water R, add 3.3 ml of buffered acetone solution R, stir for 3 min, again centrifuge, discard the supernatant liquid and repeat all the operations with the residue. Dissolve the residue using a suitable procedure, for example dissolve in 0.1 M hydrochloric acid to give a final volume of 2.0 ml. Determine the insulin content of the residue (R) and determine the total insulin content (T) of an equal volume of the suspension by a suitable method. Calculate the percentage of insulin not extractable with buffered acetone solution from the expression:

\[ \frac{100R}{T} \]

Total zinc: 0.12 mg to 0.25 mg per 100 IU of insulin, determined as described in the monograph on Insulin preparations, injectable (0854).

Zinc in solution: 20 per cent to 65 per cent of the total zinc is in the form of zinc in solution. Determine by the method described in the monograph on Insulin preparations, injectable (0854).

INSULIN ZINC INJECTABLE SUSPENSION (AMORPHOUS)

Insulini zinci amorphi suspensio injectabilis

Insulin zinc injectable suspension (amorphous) complies with the monograph on Insulin preparations, injectable (0854) with the amendments prescribed below.

DEFINITION

Insulin zinc injectable suspension (amorphous) is a sterile neutral suspension of bovine, porcine or human insulin complexed with a suitable zinc salt; the insulin is in a form which is practically insoluble in water.

General Notices (1) apply to all monographs and other texts 1811
Insulin zinc injectable suspension (crystalline)

**CHARACTERS**
A white suspension which on standing deposits a white sediment and leaves a colourless or almost colourless supernatant liquid; the sediment is readily resuspended by gently shaking. When examined under a microscope, the particles are seen to have no uniform shape and a maximum dimension rarely exceeding 2 μm.

**IDENTIFICATION**
Examine the chromatograms obtained in the Assay. The position of the peak due to insulin in the chromatogram obtained with the test solution corresponds to that of the principal peak in the chromatogram obtained with the appropriate reference solution.

**TESTS**

### Total zinc
0.12 mg to 0.25 mg per 100 IU of insulin, determined as described in the monograph on Insulin preparations, injectable (0854).

### Zinc in solution
20 per cent to 65 per cent of the total zinc is in the form of zinc in solution. Determine by the method described in the monograph on Insulin preparations, injectable (0854).

---

**INTERFERON ALFA-2 CONCENTRATED SOLUTION**

**Insulini zinci cristallini suspensio inyectabilis**

*Insulin zinc injectable suspension (crystalline)* complies with the monograph on Insulin preparations, injectable (0854) with the amendments prescribed below.

**DEFINITION**
Insulin zinc injectable suspension (crystalline) is a sterile neutral suspension of bovine, porcine or human insulin, complexed with a suitable zinc salt; the insulin is in a form which is practically insoluble in water.

**CHARACTERS**
A white suspension which on standing deposits a white sediment and leaves a colourless or almost colourless supernatant liquid; the sediment is readily resuspended by gently shaking. When examined under a microscope, the particles are seen to be rhombohedral crystals, the majority having a maximum dimension when measured from corner to corner through the crystal greater than 10 μm but rarely exceeding 2 μm.

**IDENTIFICATION**
Examine the chromatograms obtained in the Assay. The position of the peak due to insulin in the chromatogram obtained with the test solution corresponds to that of the principal peak in the chromatogram obtained with the appropriate reference solution.

**TESTS**

**Insulin not extractable with buffered acetone solution.** Not less than 90 per cent of the total insulin content. Centrifuge a volume of the substance to be examined containing 200 IU of insulin and discard the supernatant liquid. Suspend the residue in 1.65 ml of water R, add 3.3 ml of buffered acetone solution R, stir for 3 min, again centrifuge, discard the supernatant liquid and repeat all the operations with the residue. Dissolve the residue using a suitable procedure, for example dissolve in 0.1 M hydrochloric acid to give a final volume of 2.0 ml. Determine the insulin content of the residue (R) and determine the total insulin content (T) of an equal volume of the suspension by a suitable method. Calculate the percentage of insulin not extractable with buffered acetone solution from the expression:

\[
\frac{100R}{T} 
\]

**Total zinc:** 0.12 mg to 0.25 mg per 100 IU of insulin, determined as described in the monograph on Insulin preparations, injectable (0854).

**Zinc in solution:** 20 per cent to 65 per cent of the total zinc is in the form of zinc in solution. Determine by the method described in the monograph on Insulin preparations, injectable (0854).

---

**INTERFERON ALFA-2 CONCENTRATED SOLUTION**

**Interferoni alfa-2 solutio concentrata**

**DEFINITION**
Interferon alfa-2 concentrated solution is a solution of a protein that is produced according to the information coded by the alfa-2 sub-species of interferon alfa gene and that exerts non-specific antiviral activity, at least in homologous cells, through cellular metabolic processes involving synthesis of both ribonucleic acid and protein. Interferon alfa-2 concentrated solution also exerts antiproliferative activity. Different types of alfa-2 interferon, varying in the amino acid residue at position 23, are designated by a letter in lower case.

<table>
<thead>
<tr>
<th>Designation</th>
<th>Residue at position 23 (X23)</th>
</tr>
</thead>
<tbody>
<tr>
<td>alfa-2a</td>
<td>Lys</td>
</tr>
<tr>
<td>alfa-2b</td>
<td>Arg</td>
</tr>
</tbody>
</table>

This monograph applies to interferon alfa-2a and -2b concentrated solutions.

The potency of interferon alfa-2 concentrated solution is not less than 1.4 × 10⁸ IU per milligram of protein. Interferon alfa-2 concentrated solution contains not less than 2 × 10⁸ IU of interferon alfa-2 per millilitre.

**PRODUCTION**
Interferon alfa-2 concentrated solution is produced by a method based on recombinant DNA (rDNA) technology using bacteria as host cells. It is produced under conditions designed to minimise microbial contamination of the product.

Interferon alfa-2 concentrated solution contains not less than 20 per cent of the total interferon alfa-2 per millilitre.

**Host-cell-derived proteins.** The limit is approved by the competent authority.

**Host-cell- or vector-derived DNA.** The limit is approved by the competent authority.